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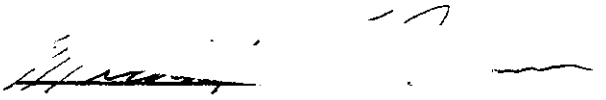

THE CHEMISTRY OF

O,N-DIARYLHYDROXYLAMINES

A THESIS

Presented to

The Faculty of the Graduate Division

by

Michael Fred Dunn

In Partial Fulfillment

of the Requirements for the Degree

Master of Science in Chemistry

Georgia Institute of Technology

June, 1963

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THE CHEMISTRY OF

O,N-DIARYLHYDROXYLAMINES

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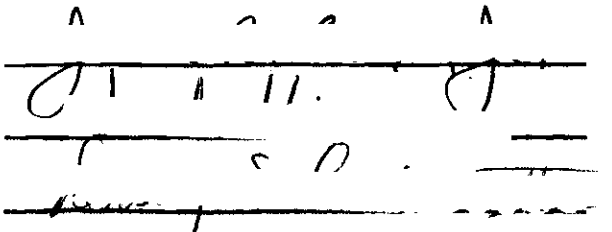

Date approved by Chairman: 31-V-63

PREFACE

O,N-Diarylamines still remain a class of unknown compounds. However, the research described in this thesis is an introduction to the interesting chemistry associated with this theoretical class of compounds.

I gratefully acknowledge my indebtedness to Dr. James R. Cox, Jr. for the suggestion of and his continued interest in this research. I am grateful also to Professor J. Hine and Dr. D. S. Caine, III, who read and criticized the original manuscript; my parents Mr. and Mrs. Fred B. Dunn for their encouragement; and my wife Linda, for her preparation of the entire manuscript and for her encouragement without which this work could not have been accomplished.

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CHAPTER I

HISTORICAL BACKGROUND

Acid-catalyzed Aromatic Rearrangements

Rearrangement of groups from nitrogen to a position on the aromatic ring of N-substituted anilines is a well documented phenomenon in the chemical literature.

A variety of N-substituents have been demonstrated to "migrate" under acid catalysis to an ortho- or para-position on the aromatic ring. The more thoroughly studied examples include the rearrangement of diazoamino compounds, the Orton rearrangement of N-haloacetanilides, the rearrangement of nitroamines, and the benzidine rearrangement[1].

These rearrangements appear to be quite similar since they are all acid-catalyzed and the overall result is migration of a substituent from nitrogen to a ring position. However, the similarity of these transformations ends with that of the overall result. The mechanisms of these trans-

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(1) For a review of acid-catalyzed aromatic rearrangements see E. D. Hughes and C. K. Ingold, Quart. Rev. (London) 6, 34 (1952) and G. W. Wheland, "Advanced Organic Chemistry", third ed., J. Wiley and Sons, Inc., New York, 1960, pp. 648 ff.

formations have been shown to differ immensely. Examples of both inter- and intramolecular pathways have been characterized and the rearrangements have been classified on this basis[1]. The variation of mechanisms which has been found to exist within each class is of further interest.

The acid-catalyzed rearrangement of aryldiazoamino compounds to aminoazobenzenes[2] is clearly an intermolecular rearrangement[3]. Kinetic studies[4] show the reaction to be first-order in substrate and of variable order in acid depending upon the acid used. The dependence in acid changed from first- to second-order as the nucleophilicity of the conjugate base of the acid increased. This was interpreted[1] to mean that the transition state involves a nucleophile as well as a proton. When a strong acid is employed the tendency toward first-order dependence on acid concentration results from the solvent's assuming the role of the nucleophile which participates in the transition state.

The intermolecular Orton rearrangement of N-haloacetanilides[5], which is specifically catalyzed by the

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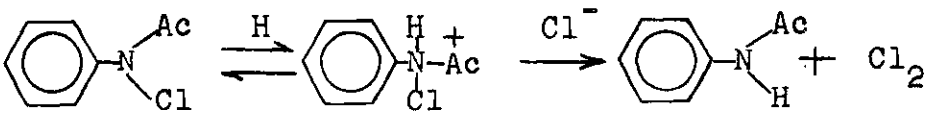
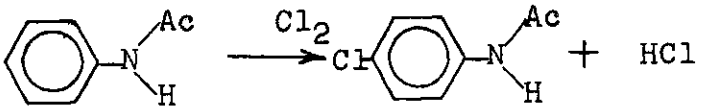
(2) P. Griess and C. A. Martius, Z. Chem., 2, 132 (1866).
(3) R. Nietzski, Chem. Ber., 10, 662 (1877).
(4) H. Goldschmidt and R. M. Salcher, Z. physik. Chem., 29, 89 (1899); H. Goldschmidt, S. Johnsen and E. Overwien, ibid, 110, 251 (1924).
(5) K. J. P. Orton and W. J. Jones, Proc. Chem. Soc., 2, 196, 223, 305 (1909); J. Chem. Soc., 95, 1456 (1909).

corresponding hydrogen halide, has been shown to exhibit a second-order dependency on acid concentration,[6] and the mechanism has been suggested to be analogous to that of the diazoamino rearrangement. In both of these examples the N-substituted aromatic amine system is protonated at nitrogen. Cleavage of the bond between the migrating group and nitrogen is brought about by attack of the nucleophile on the migrating group. The neutral aniline which results is then attacked by an electrophile, usually the migrating group, by an ordinary electrophilic substitution mechanism which effects proton displacement from the ring. This mechanism is illustrated by the Orton rearrangement of N-chloroacetanilide to p-chloroacetanilide shown below (eq. 1,2):



(1)



(2)

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(6) M. J. J. Blanksma, Rec. Trav. chim., 22, 290 (1903).

The rearrangement of N-phenylhydroxylamine discovered by Bamberger[7] is interesting in that it appears to proceed by an intermolecular mechanism quite different from the preceeding examples. The rearrangement of N-phenylhydroxylamines in aqueous sulfuric acid yields o- and p-aminophenols. In ethanolic and methanolic solutions however, the corresponding o- and p-ethoxy- and methoxyanilines are the major product, and when hydrcchloric acid in aqueous solution is employed some o- and p-chloroanilines are formed[7]. These products are best rationalized on the basis of a modification of Bamberger's original proposal, as suggested by Heller, Hughes, and Ingold[8]. Their mechanism (eqs. 3-6) differs from that of Bamberger in that a hydrogen atom is bonded to nitrogen in the intermediate (eq. 4). In these equations B:H is the conjugate acid of the attacking nucleophile.

Heller, Hughes and Ingold suggest that loss of water need not proceed by an S_N1 mechanism and they allow for the possibility of S_N2' attack at a ring position with loss of water. No work has appeared in the literature so far to distinguish between the two mechanisms. Clearly the rate of the S_N2' process should be increased if the nucleophilicity

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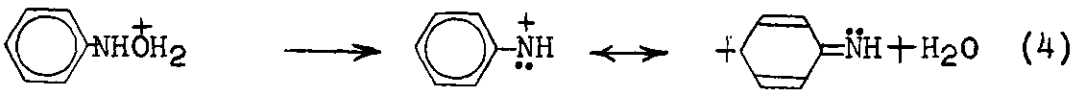
(7) E. Bamberger, Chem. Ber., 27, 1347, 1548 (1894).
(8) H. E. Heller, E. D. Hughes and C. K. Ingold, Nature, 168, 909 (1951).

of the attacking species is increased. Bamberger also reported the formation of 4'-hydroxy-4-biphenylamine when N-phenylhydroxylamine was rearranged in the presence of phenol and sulfuric acid[7]. Heller, Hughes and Ingold[8] suggest that this product arises from the same pathway using phenol as a nucleophile to react with the active electrophilic intermediate.

(3)



(4)

(5)

(6)

The validity of generalizing the mechanism to include the formation of this biphenyl derivative is in serious question, and in view of the results to be set forth in this

thesis, an equally valid possibility seems to be the formation of O,N-diphenylhydroxylamine followed by an acid-catalyzed intramolecular rearrangement similar to the benzidine rearrangement. Further experiments to test these possibilities must be devised.

The rearrangement of arylnitroamines[9] has been shown to occur via an intramolecular pathway[10] under ordinary conditions of acid catalysis, but when a deactivated nitroamine is rearranged in the presence of a more reactive foreign molecule[10], nitration of the foreign molecule is found to accompany rearrangement. Thus it appears that in the case of nitroamines the rearrangement may proceed by either an intra- or intermolecular pathway depending upon the system under consideration.

The most interesting and most carefully studied of these rearrangements is that of hydrazobenzene to benzidine. The benzidine rearrangement was discovered by Hofmann in 1863[11], who observed that the reduction of azobenzene with ammonium sulfide formed an unstable intermediate isomeric

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(9) E. Bamberger and K. Landsteiner, Chem. Ber., 26, 482 (1893); E. Bamberger, ibid, 27, 359 (1894); ibid, 30, 1248 (1897).

(10) E. D. Hughes and G. T. Jones, J. Chem. Soc., 2678 (1950).

(11) A. W. Hofmann, Proc. Roy. Soc., (London), 12, 576 (1863).

with benzidine and easily convertible to benzidine on treatment with mineral acids. Hofmann's intermediate, hydrazobenzene, has since been found to give on rearrangement, benzidine (approximately 70 per cent), diphenyline[12] (approximately 30 per cent) and trace amounts of o-semidine (0.3 per cent), p-semidine (1.0 per cent) and o-benzidine (9.3 per cent)[13] as well as some aniline and azobenzene from an autooxidation-reduction process.

Smith, Schwartz and Wheland[14] conclusively demonstrated that benzidine rearrangements of 2,2'-dimethylhydrazobenzene and 2-methylhydrazobenzene are entirely intramolecular, and Hammond and Shine[15] found that the reaction of hydrazobenzene is third-order, second-order in hydrogen ions and first-order in substrate, and probably is subject to general Brønsted acid catalysis.[15] Interpretation of these facts suggests a mechanism which requires a second

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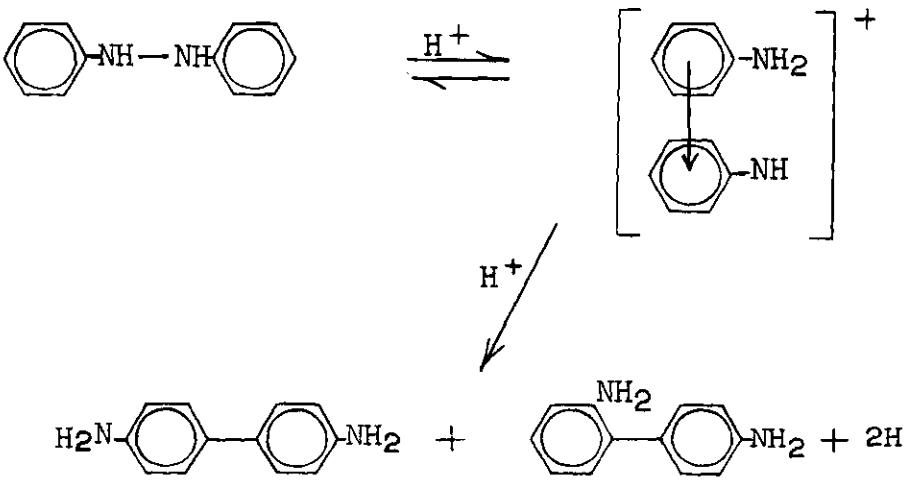
(12) H. Schmidt and G. Schultz, Chem. Ber., 11, 1754 (1878).

(13) Conflicting reports on the products of the benzidine rearrangement of hydrazobenzene are in the literature. See R. B. Carlin, R. G. Nelb and R. C. Odioso, J. Am. Chem. Soc., 73, 1002 (1951), versus M. Večeřa, J. Petránek, and J. Gasparič, Collection Czech. Chem. Commun. 22, 1603 (1957).

(14) D. H. Smith, J. R. Schwartz, G. W. Wheland, J. Am. Chem. Soc., 74, 2282 (1952).

(15) G. S. Hammond, H. J. Shine, J. Am. Chem. Soc., 72, 220 (1950).

protonation before or during the rate-determining step of the rearrangement. Dewar,[16] Hammond and Clovis,[17] Hughes and Ingold[18] and others have proposed several mechanisms which take these facts into account. Dewar's[16] π-complex mechanism, illustrated below, in light of recent molecular orbital calculations[19] appears to be the most attractive mechanism within the framework of the present information.



(7)

(16) M. J. S. Dewar, "Electronic Theory of Organic Chemistry", Oxford Press, London, 1949, pp. 235-240; "Kekulé Symposium on Theoretical Organic Chemistry", Butterworth's Scientific Publications, London, 1958, pp. 190 ff.

(17) G. S. Hammond and J. S. Clovis, Tetrahedron Letters, 1962, 945.

(18) E. D. Hughes and C. K. Ingold, J. Chem. Soc., 608 (1941); C. A. Bunton, C. K. Ingold and M. M. Mhala, ibid, 1906 (1957); D. V. Banthorpe, C. K. Ingold, J. Roy and S. M. Sommerville, ibid, 2436 (1962).

(19) L. C. Snyder, J. Am. Chem. Soc., 84, 340 (1962).

The observation that o-hydrazotoluene[20] and certain other hydrazobenzenes exhibit apparent orders in hydrogen ion concentration varying from one to two complicate the situation but may be rationalized in terms of the following mechanism and rate expression first proposed by Blackadder and Hinshelwood:[21]

$$PhNHNHPh + H^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} PhN\overset{+}{H}_2NHPh + H^+ \xrightarrow{k_3} \text{product} \qquad (8)$$

$$PhN\overset{+}{H}_2NHPh \xrightarrow{k_2} \text{product} \qquad (9)$$

$$-\frac{d[PhNHNHPh]}{dt} = \frac{k_1}{k_{-1}}[PhNHNHPh][H^+](k_3[H^+] + k_2) \qquad (10)$$

This scheme predicts a limiting first-order dependency at low hydrogen ion concentrations and a second-order dependency at higher concentrations since at low enough concentrations the squared term in hydrogen ion concentration becomes negligible. This treatment allows rearrangement of the monoprotonated form as an independent pathway. This seems reasonable in view of the thermally induced benzidine

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(20) R. B. Carlin and R. C. Odioso, J. Am. Chem. Soc., 76, 100 (1954).

(21) D. A. Blackadder and C. Hinshelwood, J. Chem. Soc., 2898 (1957).

rearrangements studied by Shine and Trinsler[22] which require no hydrogen ion *per se*.

The monoprotonated π-complex proposed by Dewar[16] is not rigorously required by the known facts. However, in the absence of π-interaction, the two rings cannot approach to within less than about 3.7Å (the "thickness" of a benzene ring) in a roughly parallel configuration. If each ring has a positive charge prior to the transition state as suggested by some, then the distance between the rings should be somewhat greater; separation into fragments and occurance of intermolecular processes would then seem as likely as intramolecular bond formation.

The benzidine rearrangement is not confined to substituted benzenes. A similar rearrangement takes place when *p*-quinamines are treated with acid, the rearrangement having been shown to be intramolecular and first-order in both substrate and hydrogen ion.[23] Beyer, *et. al.*,[24] have found examples of benzidine-like rearrangements with 2-phenylhydrazinopyridine, 2-phenylhydrazino-6-methylpyridine,

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(22) H. J. Shine and J. C. Trisler, *J. Am. Chem. Soc.*, 82, 4054 (1960).

(23) B. Miller, *Tetrahedron Letters*, 1962, 255.

(24) H. Beyer, H. J. Haase and W. Wildgrube, *Chem. Ber.*, 91, 247 (1958); T. Pyl, H. Lahner and H. Beyer, *ibid*, 94, 3217 (1961).

2,2'-bis-phenylhydrazinobithiazolyl-(4,4'), and 2-phenylhydrazinoimidazole. Beyer has not demonstrated the intramolecularity of these rearrangements but it is very likely that closer examination will confirm the deduction that these, too, are of benzidine-like nature.

O,N-Diarylhydroxylamines

The general nature of the benzidine rearrangement and the acid-catalyzed lability of the nitrogen-nitrogen single bond in hydrazo compounds is of considerable theoretical interest. Analogues of the benzidine rearrangement, as well as being of considerable theoretical interest in their own right, may well lend insight into the anomalies which remain unresolved in the benzidine rearrangement. The work set forth in this thesis is directed toward exploration of such analogues with these ends as its justification. This research was initiated with the intention of synthesizing members of the unknown class of compounds, O,N-diarylhydroxylamines, and investigating their behavior in an acidic environment.

Since O,N-diarylhydroxylamines are unknown, the chemical literature is exceedingly sparse on this subject. However, in two reactions reported by Bamberger the products suggest that O,N-phenylhydroxylamine may possibly have been

a reaction intermediate. 4'-Hydroxy-4-biphenylamine was formed from N-phenylhydroxylamine, phenol and sulfuric acid.[7] The same product was isolated when azidobenzene was boiled under reflux with phenol in aqueous sulfuric acid.[25] Bamberger interpreted both reactions in terms of a univalent nitrogen intermediate Ph-N. Hughes and Ingold[18] have reinterpreted the N-phenylhydroxylamine reaction in terms of the electrophilic intermediate $Ph-\overset{+}{N}H$. The alternative interpretation that O,N-diphenylhydroxylamine was formed as the reactive intermediate and rearranged intramolecularly appears to be as valid as that of Hughes and Ingold, based on existing evidence.

The formation of 4'-hydroxy-4-biphenylamine from the decomposition of both azidobenzene and N-phenylhydroxylamine in the presence of phenol may very likely proceed *via* the common electrophilic intermediate $Ph-\overset{+}{N}H$ discussed above. The mechanisms of azide decompositions are not clearly understood, Smolinsky[26] has investigated the thermal decomposition of various *ortho*-substituted azidobenzenes both in the vapor phase and in solution and he suggests that decomposition occurs *via* an aryl azene intermediate. Smolinsky also

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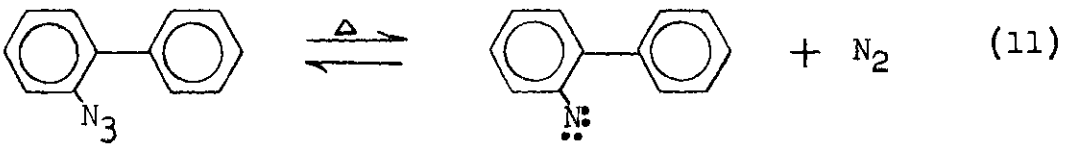
(25) E. Bamberger, *Ann.*, 443, 192 (1925).
(26) G. Smolinsky, *J. Org. Chem.*, 26, 4108 (1961); *J. Am. Chem. Soc.*, 82, 4717 (1960); *ibid*, 83, 2489 (1961).

suggests, in order to explain the observed reaction paths of hydrogen abstraction, carbon-hydrogen bond insertion and azo bond formation, that the intermediate azene is formed in a triplet state with diradical character. Smith and Hall[27] have studied the kinetics of the thermal decomposition of o-azidobiphenyls in decalin to yield the corresponding carbazoles. They also suggest that the reaction proceeds via an aryl azene intermediate illustrated by the following sequence (eqs. 11,12):



(11)

(12)

It has been demonstrated by Newman and co-workers[28] that the Curtius reaction is subject to acid catalysis. They suggest that catalysis is effected by protonation at

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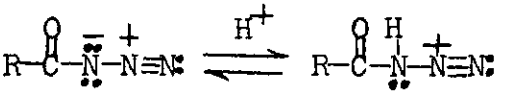
(27) P. A. S. Smith and J. H. Hall, J. Am. Chem. Soc., 84, 480 (1962).

(28) M. S. Newman and H. L. Gildenhorn, J. Am. Chem. Soc., 70, 317 (1948); R. A. Coleman, M. S. Newman and A. B. Garrett, ibid, 76, 4534 (1954).

the ∝-nitrogen, followed by migration of the R group as shown below, (eqs. 13-15), displacing nitrogen.



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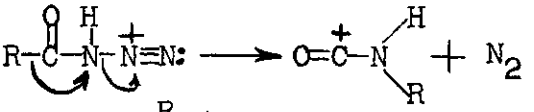

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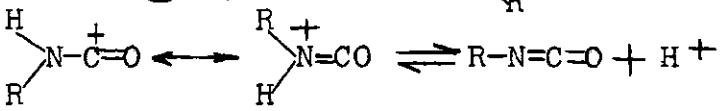
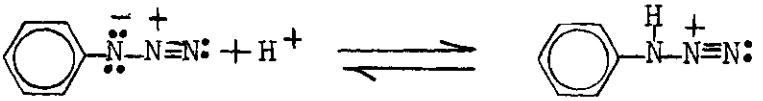


(15)

However, protonation at the carbonyl oxygen followed by migration of the R group appears to be an equally likely pathway.[29]

In Bamberger's reaction of azidobenzene with phenol and sulfuric acid it appears likely that the azide decomposition takes place in the following manner, (eqs. 16,17):



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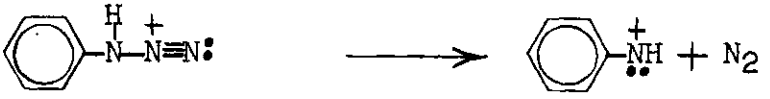

(17)

yielding the same intermediate suggested for the reaction between N-phenylhydroxylamine and phenol.

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(29) J. Hine, "Physical Organic Chemistry", second ed., McGraw Hill Inc., Maple Press Co., York, Pa., 1962, pp. 336 ff.

CHAPTER II

EXPERIMENTAL

Instrumentation

A modified Hershberg melting point apparatus fitted with a motor driven stirrer and equiped with Anschütz thermometers was used for all melting points below 230° using the open capillary tube method. A Fisher-Johns hot stage was used above 230°.

All infrared spectra were taken on the Perkin-Elmer Infracord spectrophotometer using sodium chloride plates, and were calibrated with the 6.238μ band of polystyrene. All NMR spectra were obtained on the Varian Associates Model A-60 spectrometer using internal standards of tetramethylsilane for organic solvents and sodium 2,2-dimethyl-2-silapentane-5-sulfonate for aqueous systems.

Benzenediazonium-2-carboxylate[30]

Anthranilic acid was diazotized essentially by the

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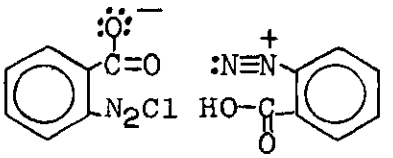
(30) Both solid benzene diazonium-2-carboxylate and its solutions have been observed to detonate from rubbing or from mild heating; thus as a safety precaution the use of polyethylene equipment is strongly recommended, as is the use of a protective shield.

Procedure of Hantzsch and Davidson.[31] Five grams (0.04 mole) was dissolved in 50 ml. of absolute ethanol followed by the addition of 5 ml. of concentrated hydrcchloric acid. The solution was cooled to 0-5° in a salt-ice slurry, whereupon anthranilic acid hydrochloride precipitated. The drop-wise addition of 5 g. (0.043 mole) of n-butyl nitrite to the stirred mixture resulted in solution of the crystalline hydrochloride salt. Ten milliters of concentrated hydrochloric acid was then added in one portion followed by the addition of 50 ml. of ethyl ether, whereupon the diazotized anthranilic acid precipitated as the semi-chloride dimer[31] (I) in nearly quantitative yield.



(I)

The white needles decomposed on prolonged storage at refrigerator temperatures.

The semi-chloride dimer was dissolved in 50 ml. of dry methanol, and silver oxide was added in small portions with magnetic stirring until complete removal of hydrochloric

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(31) A. Hantzsch and W. B. Davidson, Chem. Ber., 29, 1535 (1896).

acid was evidenced by the persistence of the brown silver oxide coloration in the stirred mixture. The mixture was then filtered over activated charcoal, and 500 ml. of cold, dry ether was added to the almost colorless filtrate at zero degrees. Glistening, almost white leaflets of free benzenediazonium-2-carboxylate precipitated. Benzenediazonium-2-carboxylate should be used as soon as possible after isolation since it rapidly decomposes at room temperature and cannot be stored satisfactorily even at -5°.

N-Phenylhydroxylamine

N-Phenylhydroxylamine was conveniently prepared by the reduction of nitrobenzene with zinc dust in an aqueous ammonium chloride buffer.[32]

N-Acetylphenylhydroxylamine

N-Acetylphenylhydroxylamine was prepared by the method of Bamberger[33] except that acetylation of phenylhydroxylamine with the stoichiometric amount of acetic anhydride was accomplished in ethereal solution at 0° rather than in water. The product recrystalized from benzene as glistening white leaflets, m.p. 65.5-66.5° (reported,[33] m.p. 67°).

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(32) O. Kamm, Organic Syntheses, Col. Vol. I, ed. 2, J. Wiley and Sons Inc., N. Y., 1941, pp. 445 ff.

(33) E. Bamberger, Chem. Ber., 51, 637 (1918).

N-Acetylphenylhydroxylamine appeared to be quite stable at refrigerator temperatures, as after ten months no decomposition was evident.

Reaction of Benzenediazonium-2-carboxylate with N-Acetylphenylhydroxylamine

Freshly prepared benzenediazonium-2-carboxylate (5 g., 0.036 mole) was added slowly in small portions as the solid to N-acetylphenylhydroxylamine (5 g., 0.033 mole) dissolved in 75 ml. of distilled, dry benzene. Upon addition of a small portion of the diazonium compound the solution took on a green color and gas was evolved smoothly. The solution darkened to a red-brown color within the space of a few minutes, with the formation of a red-brown tar which also evolved gas. The products from 4 such reactions were combined and allowed to stand overnight. The resulting mixture was then filtered and evaporated *in vacuo* to a red-brown oil. When this oil was placed under 0.5 mm. vacuum for further drying at room temperature it was noticed that white needles, m.p. 120-121°, sublimed from the tar. Sublimation of the tar, 70-100°/0.5 mm. yielded light yellow needles, m.p. 95-105° which recrystalized from carbon tetrachloride, yielding more of the material melting at 121-122°. Further sublimation at 150-180° yielded a yellow-orange solid, m.p.

105-110°, which recrystalized from carbon tetrachloride as a white solid, m.p. 114°.

The material melting at 121-122° was shown to be identical with benzoic acid (reported, 123°) by mixed melting point (no depression) and the superimposibility of its infrared and NMR spectra in carbon tetrachloride upon those of an authentic sample.

The benzene-insoluble tar, when sublimed, yielded more benzoic acid and acetanilide. The remainder of the reaction products appeared to be polymeric materials not readily identified.

Iodyl Sulfate

Iodyl sulfate was prepared by the method of Masson and Hanby[34] by vigorously stirring stoichiometric quantities of finely divided iodine (2 mole) and potassium or sodium iodate (6 mole) in an excess of concentrated sulfuric acid (15 mole) until the mixture had become a bright yellow. The iodyl sulfate was isolated as a yellow solid by filtration through a fritted glass funnel.

Diphenyliodonium Bisulfate

Diphenyliodonium bisulfate was prepared by the method

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(34) I. Masson and W. E. Hanby, J. Chem. Soc., 1718 (1937).

of Beringer[35] by the addition of 40 g. (0.513 mole) of benzene dropwise to a stirred mixture of 0.083 mole iodyl sulfate in 100 ml. concentrated sulfuric acid and 15 ml. acetic anhydride at 0-5°. After addition was complete, the mixture was stirred for six hours during which time it was allowed to warm slowly to room temperature. The solution was then diluted with 500 ml. of dry ether, whereupon a black residue precipitated which was removed by filtration. Further dilution with dry ether precipitated diphenyliodonium bisulfate as a brown solid. Purification was found to be effected best by washing the precipitated material with acetone. After several washings the diphenyliodonium bisulfate was obtained as a white solid which decomposes at 170-171.5° (reported,[35] 164-166°), in 41 per cent of theory. The ultraviolet spectrum indicated that the material was better than 99 per cent pure (λ_{max} = 227.5 mμ ; ϵ = 1.43 ± 0.02 x 10^4 l. cm.$^{-1}$ mole^{-1}).[36]

Stability of Diphenyl Iodonium Hydroxide in Aqueous Solution

A solution of diphenyliodonium hydroxide was prepared

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(35) F. M. Beringer, M. Drexler, E. M. Gindler and C. C. Lumpkin, J. Am. Chem. Soc., 75, 2905 (1953), and also F. M. Beringer, R. A. Falk, M. Karniol, I. Lillien, G. Masullo, M. Mausner, E. Sommer, ibid, 81, 342 (1959).

(36) H. Irving, G. P. A. Turner, and R. W. Reid, J. Chem. Soc., 2082 (1960).

by dissolving 5.6728 g. (0.015 mole) of the bisulfate in approximately 50 ml. water and then adding 78 ml. of 0.394 N barium hydroxide. The precipitated barium sulfate was removed by filtration and the diphenyliodonium hydroxide solution was stored in a polyethylene bottle at room temperature. This solution was titrated with 0.217 N sulfuric acid at intervals over several days to yield the data in table 1.

Table 1. Decomposition Rate of Diphenyliodonium Hydroxide

ml. H_2SO_4 per 10 ml. Solution	Time (hrs.)
5.88	0.50
6.02	3.00
6.00	9.75
5.83	20.50
5.85	28.00
5.65	45.50
5.25	95.25

Reaction of Diphenyliodonium Hydroxide with N-Acetylphenylhydroxylamine

A solution of 0.010 moles of diphenyliodonium hydroxide was prepared by adding 52 ml. of 0.394 N barium hydroxide to 3.800 g. (0.010 mole) of diphenyliodonium bisulfate in the reaction degassing apparatus (fig. 1). Next 1.512 g.

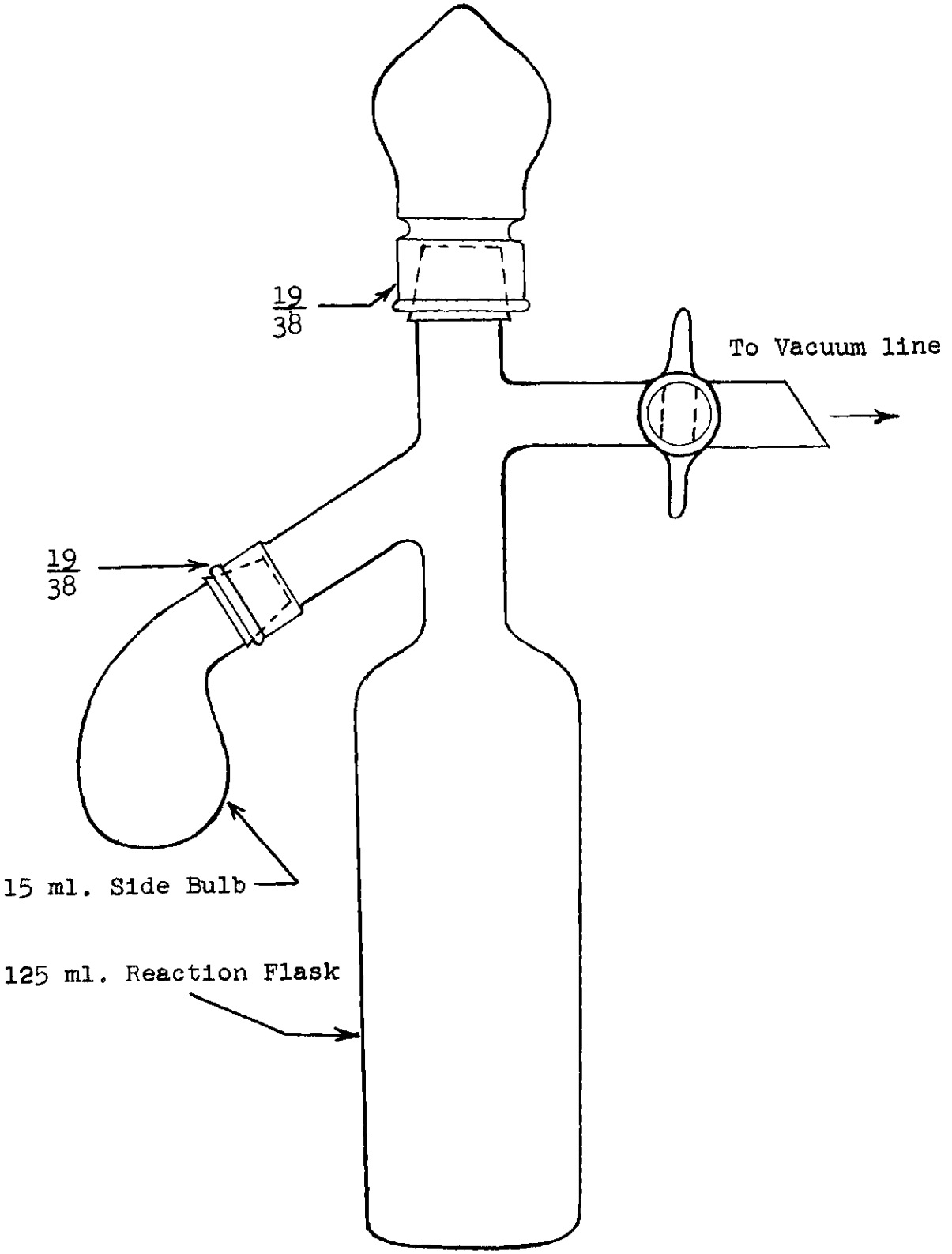

Figure 1. Reaction Degassing Apparatus

(0.010 mole) of N-acetylphenylhydroxylamine was placed in the small side bulb of the apparatus. The diphenyliodonium hydroxide solution was scrupulously degassed by freezing the solution in a Dry Ice-acetone slurry and thawing under a moderately high vacuum, the procedure being repeated until there were no visible gas bubbles occluded in the frozen solution.

When degassing of the solution was complete, the N-acetylphenylhydroxylamine was added to the solution by inverting the apparatus and shaking. Upon mixing the solution turned pale yellow in color.[37] After five hours at room temperature, a dark red, oily precipitate was observed to have formed on the walls of the reaction apparatus. After 48 hrs. the reaction solution was carefully transferred under vacuum to an evacuated, 250 ml. single-necked, round-bottom flask, leaving behind the precipitated material. From the supernatant solution there precipitated a negligible amount of material on standing for several days, indicating that the reaction was essentially complete in 48 hrs. The dark red, oily precipitate remaining in the reaction apparatus was dried in the apparatus for approximately 20 hrs.

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(37) When this reaction is run in the presence of oxygen the solution turns to an intense blue color.

under a vacuum of 0.1 mm. at room temperature. Iodobenzene (0.40 g.) was recovered from the vacuum line trap in 19.6 per cent of theory. The solid residue in the apparatus (infrared spectrum fig. 2) was washed from the apparatus with approximately 100 ml. of distilled chloroform and filtered to yield a tan residue containing some barium sulfate. The barium sulfate was removed by extracting the organic material with excess chloroform and filtering off the barium sulfate. The supernatant chloroform solution was evaporated in vacuo yielding 0.68 g. of a tan material which was recrystalized from hot ethanol as almost white needles, m.p. 226.0-226.6° (infrared spectrum fig. 3). The 100 ml. chloroform extract (above) was evaporated in vacuo to yield after drying under vacuum (0.5 mm.) 1.25 g. of a red-brown, semi-solid material (infrared spectrum fig. 4). The NMR of this material indicated the presence of an acetyl methyl group, τ = 7.9 (relative to TMS), and the presence of aromatic protons, τ = 2.8. An attempt to purify this material by vacuum sublimation at 200°/0.5mm. met with no success. The material was then chromatographed over neutral alumina (100-200 mesh), by eluting with distilled chloroform, 50 per cent chloroform-methanol, methanol and 50 per cent methanol-water. The eluted fractions when evaporated in vacuo yielded only red

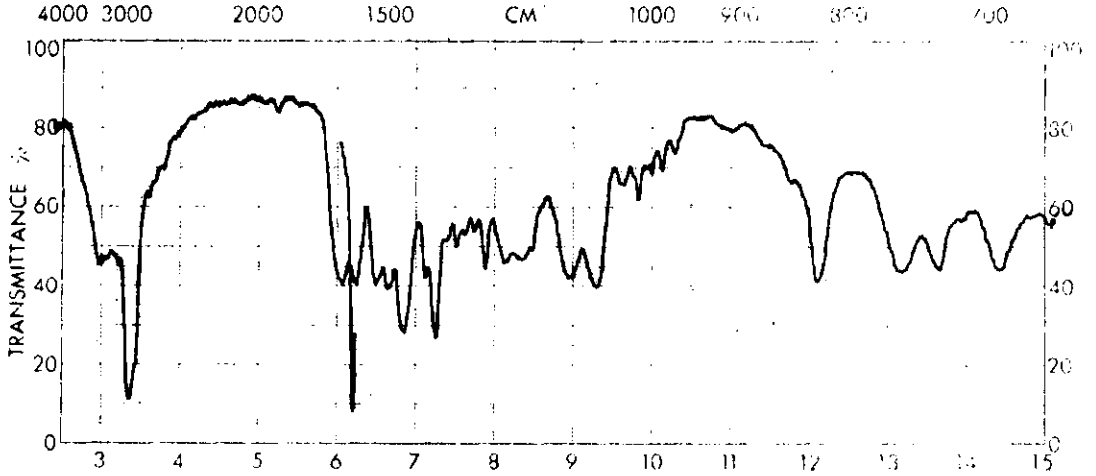

Figure 2. Reaction of Diphenyliodonium Hydroxide with N-Acetylphenylhydroxylamine (Crude, Nujol)

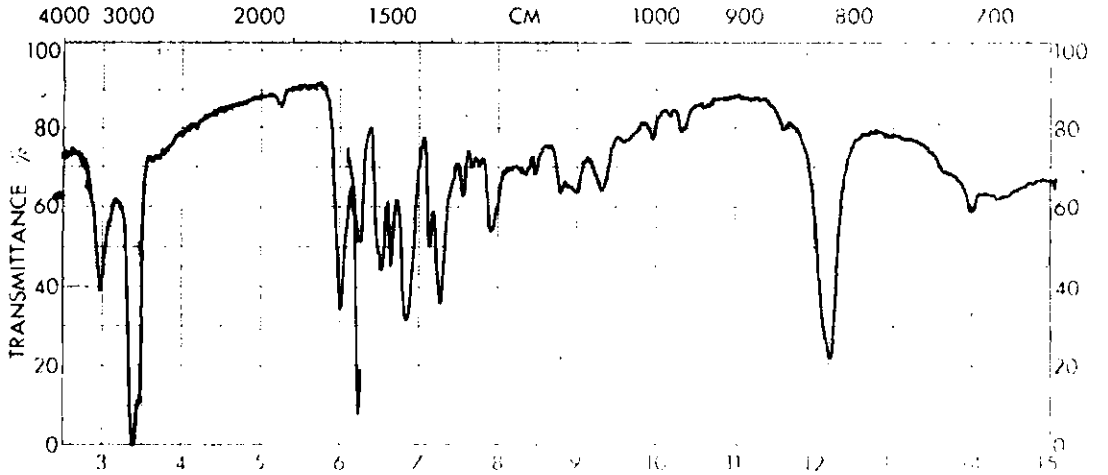

Figure 3. 4-Hydroxy-4'-N-acetylbiphenylamine from the Reaction of Diphenyliodonium Hydroxide with N-Acetylphenylhydroxylamine (Nujol)

tars which could not be identified. However, when the chloroform soluble portion of the reaction mixture from another preparation was chromatographed over neutral alumina prior to attempted sublimation there was obtained a light tan material in as high as 9.4 per cent yield, m.p. 196-197°.

The material melting at 226.0-226.6° was found to be identical with 4'-hydroxy-4-N-acetylbiphenylamine (reported,[38] m.p. 224-225°) on the basis of the following evidence. A mixed melting point with an authentic sample was undepressed and their infrared spectra were superimposible (figs. 3,5). The O,N-diacetyl derivatives were prepared and were similarly identical with m.p. and m.m.p. of 222-223° (reported,[38] 219-220°) and superimposible infrared spectra (figs. 6,7). The corresponding 4'-hydroxy-4-biphenylamine from hydrolysis in hot 6 N sodium hydroxide was also found to be identical with an authentic sample, with m.p. and m.m.p. 260-265° dec. (reported,[38] 270° dec.) and superimposible infrared spectra (figs. 8,9).

The material melting at 196-197° was tentatively identified as 2'-hydroxy-4-N-acetylbiphenylamine on the basis of its melting point (reported,[39] 198-199°) and the

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(38) L. C. Raiford and E. P. Clark, J. Am. Chem. Soc., 48, 483 (1925).

(39) C. Finzi, Gazz. chim. Ital., 61, 33 (1931).

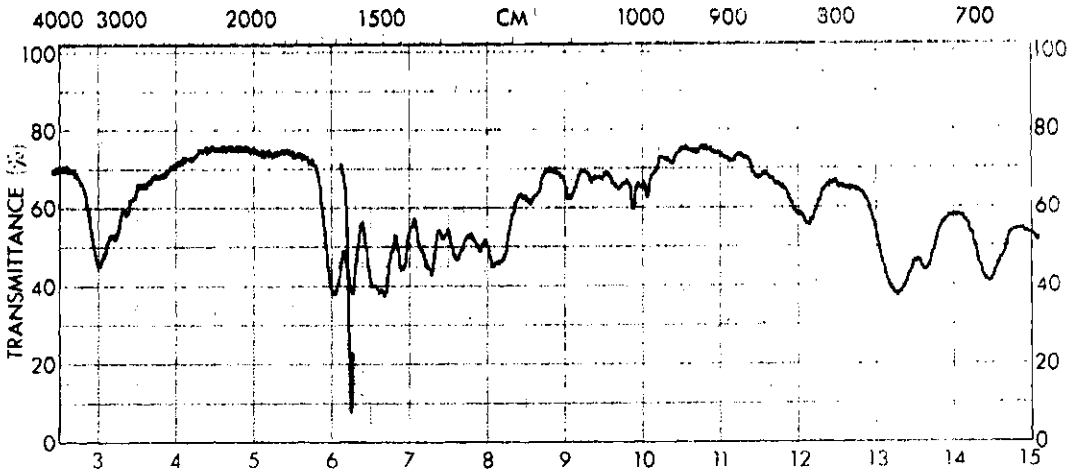


Figure 4. Chloroform Soluble Material from the Reaction of Diphenyliodonium Hydroxide with N-Acetylphenylhydroxylamine (Neat)

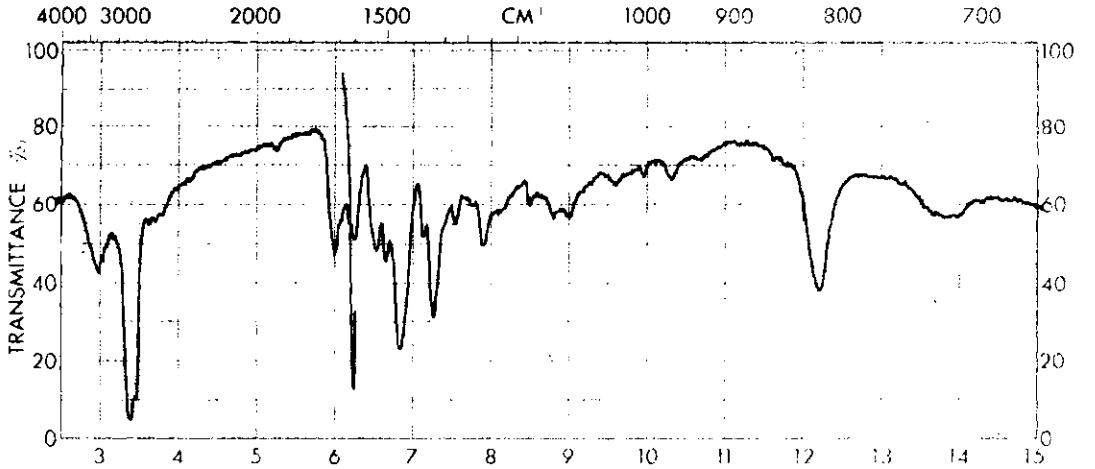


Figure 5. Authentic 4-Hydroxy-4'-N-acetylbiphenylamine (Nujol)

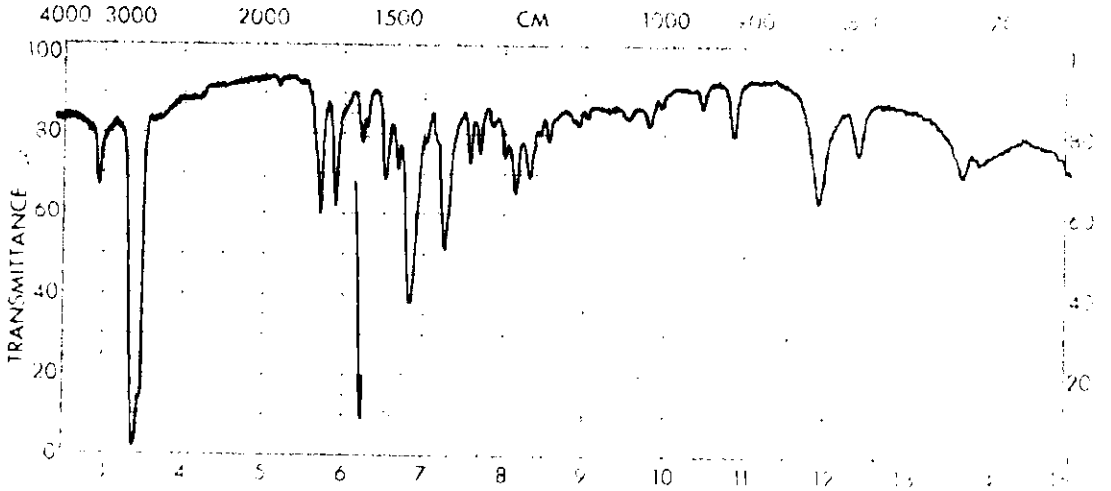


Figure 6. 4-Acetoxy-4'-N-acetylbiphenylamine (Nujol)

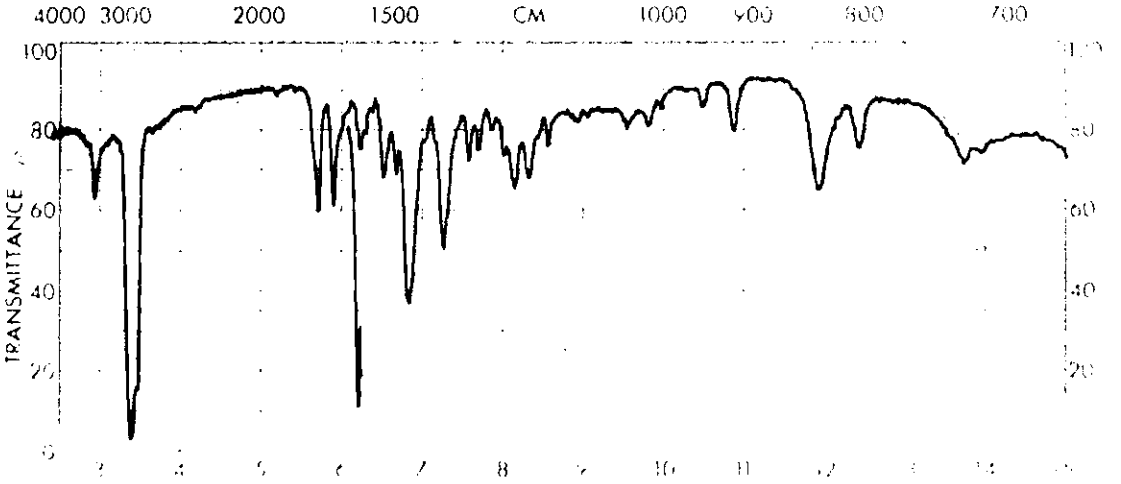


Figure 7. Authentic 4-Acetoxy-4'-N-acetylbiphenylamine (Nujol)

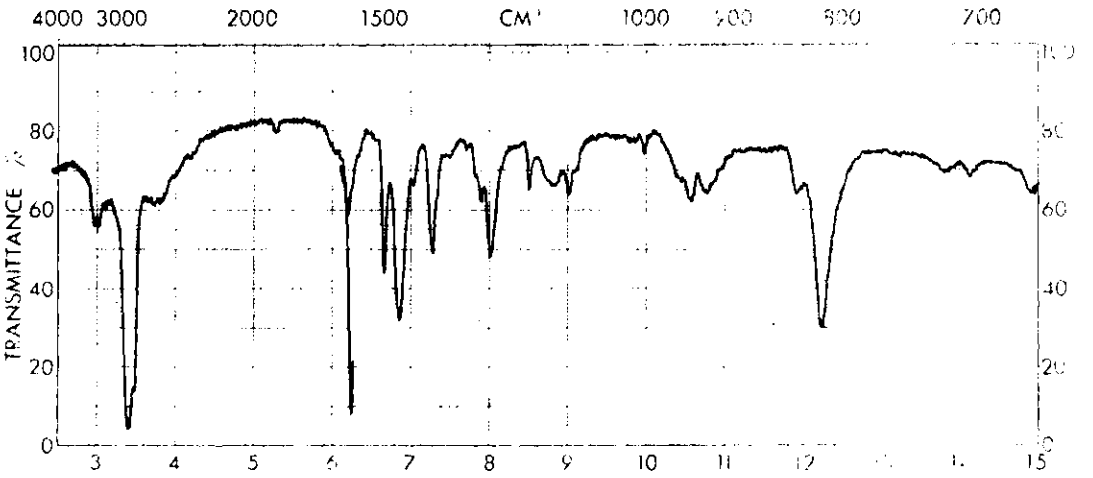


Figure 8. 4-Hydroxy-4'-biphenylamine (Nujol)

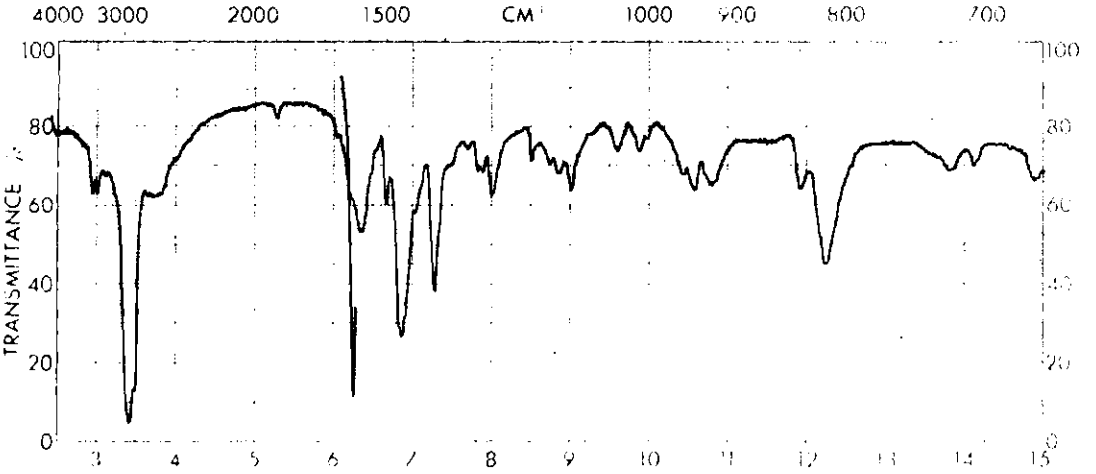
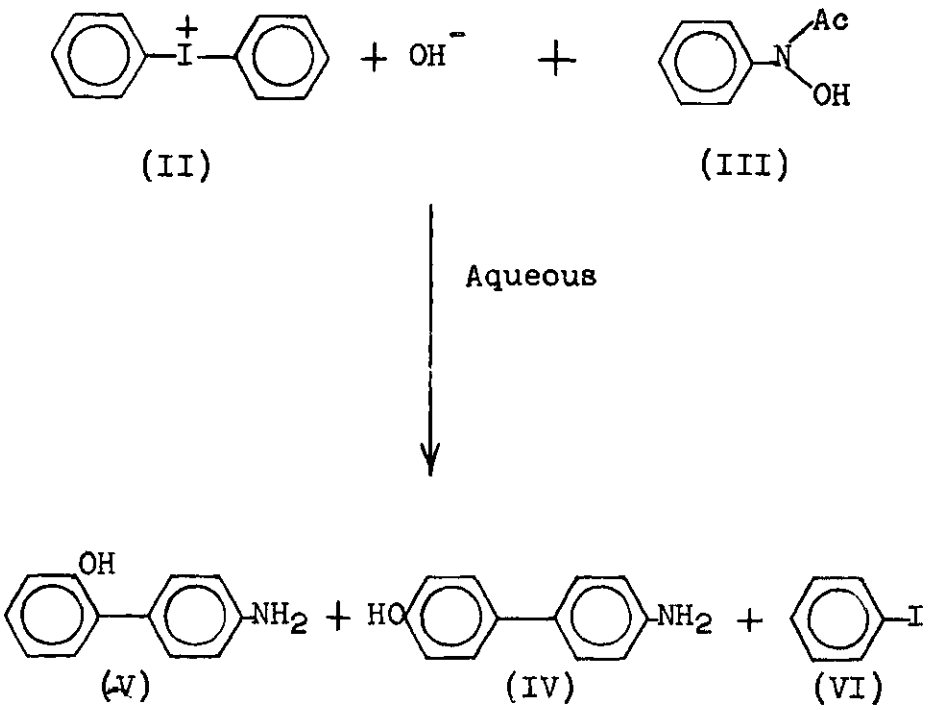


Figure 9. Authentic 4-Hydroxy-4'-biphenylamine (Nujol)

close similarity of its infrared spectrum (fig. 10) to that of its 4'-hydroxy isomer. Table 2 summarizes the results of three reactions of diphenyliodonium hydroxide with N-acetylphenylhydroxylamine.

Table 2. Reaction of Diphenyliodonium Hydroxide with N-Acetylphenylhydroxylamine



Reaction	Moles, Reactant (II)	(III)	O_2	Per Cent Product (IV)	(V)	(VI)
1	0.0282	0.0282	Present	8.6	9.4	----
2	0.020	0.020	Present	6.6	10.0	----
3	0.020	0.020	Absent	30.0	----	19.6

4'-Hydroxy-4-N-acetylbiphenylamine

A mixture of 17.4 g. (0.146 mole) azidobenzene,[40,41] 54.4 g. (0.586 mole) phenol and 50 g. concentrated sulfuric acid in 250 ml. water was stirred at reflux temperature. After 20 hrs. there could be seen suspended in the black reaction mixture silver platelets of a crystalline material. Filtration, followed by washing with acetone, yielded 2.55 g. (8.9 per cent) of the 4'-hydroxy-4-biphenylamine bisulfate. Neutralization of the salt in aqueous solution with sodium acetate followed by acetylation with acetic anhydride in warm basic solution yielded a light purple solid, m.p. 221-223°, purified by vacuum sublimation (220°/0.5 mm.) to a white solid, m.p. 224-225° (infrared spectrum fig. 5).

Using the above amounts of azidobenzene and phenol a modification of the procedure was investigated, eliminating water and sulfuric acid from the reaction. Heating at 160° for 19 hours was accompanied by the smooth evolution of a gas (first noticed at 100-120°); the homogeneous solution which remained after cooling was washed with 100 ml. of dilute sulfuric acid, filtered and washed with acetone yielding 0.25 g. (0.9 per cent) of the 4'-hydroxy-4-biphenylamine bisulfate. No other products were identified.

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(40) E. Bamberger, Ann., 443, 196 (1925).
(41) E. Noelting and O. Michel, Chem. Ber., 26, 86 (1893).

Reaction of Diphenyliodonium Hydroxide with N-Phenylhydroxylamine

The reaction of diphenyliodonium hydroxide with N-phenylhydroxylamine in aqueous solution in the absence of atmospheric oxygen was accomplished by dissolving 7.60 g. (0.02 mole) of diphenyliodonium bisulfate in 100 ml. water containing approximately 0.06 mole of sodium hydroxide. This solution was placed in the reaction degassing apparatus (fig. 1) and 2.18 g. (0.02 mole) of N-phenylhydroxylamine was placed in the side bulb. The solution was degassed as previously described. After degassing, the solution of diphenyliodonium hydroxide was mixed with the phenylhydroxylamine. The immediate formation of a yellow-brown oil was observed upon mixing. The reaction mixture was allowed to stand for 20 hrs. followed by extraction of the yellow-brown oil with ether. The ether extract was evaporated *in vacuo* at room temperature to yield an orange-red oil which was placed under 0.02 mm. vacuum for six hrs. at room temperature. At this time the Dry Ice-acetone trap yielded 1.91 g. of iodobenzene and the flask contained 3.8 g. of the orange-red oil. Cooling the oil overnight at refrigerator temperatures yielded a few crystals of a tan material m.p. 114-117°. Further *in vacuo* treatment of the oil for four days at room temperature

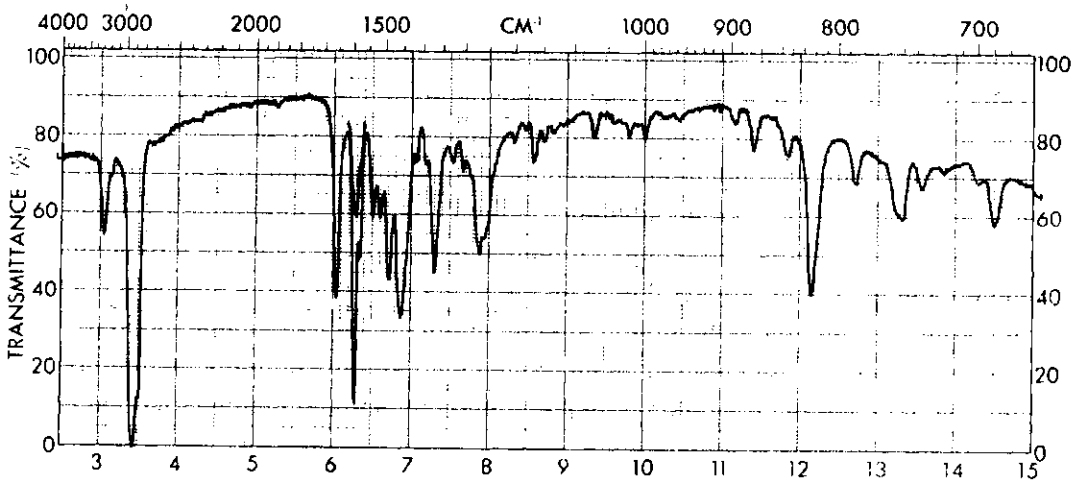

Figure 10. 2-Hydroxy-4'-N-acetylbiphenylamine from the Reaction of Diphenyliodonium Hydroxide with N-Acetylphenylhydroxylamine (Nujol)

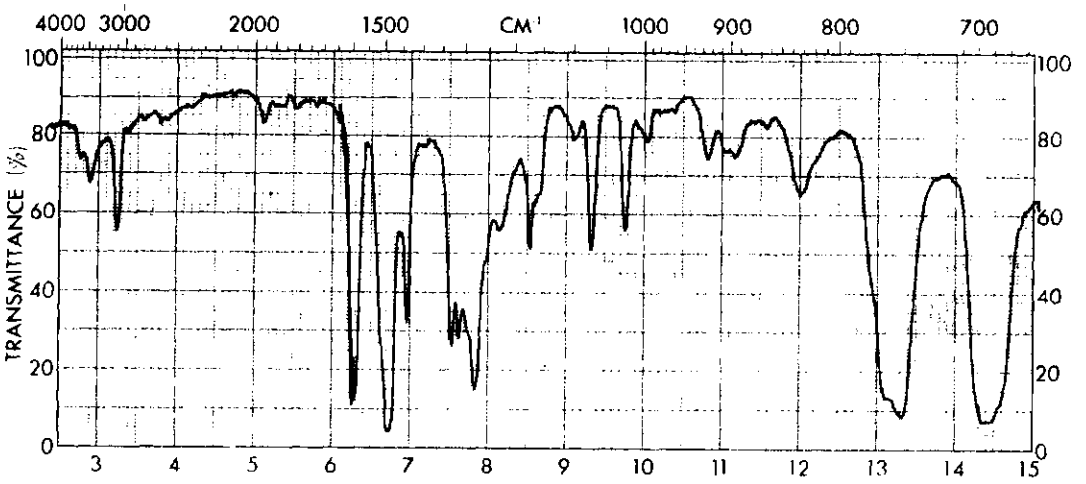

Figure 11. Reaction of Diphenyliodonium Hydroxide with N-Phenylhydroxylamine (Crude, Neat)

yielded another 1.0 g. of iodobenzene from the Dry Ice-acetone trap, and a semi-solid residue remained in the flask (infrared spectrum, fig. 11). The residue when filtered through fritted glass yielded 0.31 g. of a dark brown solid and 1.32 g. of a dark brown, viscous, oily filtrate (infrared spectrum, fig. 12). The solid residue was chromatographed with benzene over a neutral alumina column (1X20 cm., 100-200 mesh), to yield after evaporation in vacuo 0.25 g. of light yellow crystals, m.p. 109-115°. When this material was washed with cold, low boiling petroleum ether, a white crystalline material was obtained, m.p. 125-126°. This material recrystalized from warm benzene as colorless prisms, and from warm petroleum ether as colorless star-shaped crystals m.p. 126.0-126.5° (infrared spectrum fig. 13).

This material was shown to be identical with triphenylamine on the basis of its melting point (reported, 126.5°), interpretation of its infrared spectrum, its crystalline form and its solubility characteristics.

The dark brown oily filtrate was similarly chromatographed over neutral alumina with the use of benzene, benzene-chloroform, chloroform, chloroform-methanol and methanol as eluents in the order listed. The various fractions obtained when evaporated in vacuo yielded black tars which have not as yet been identified.

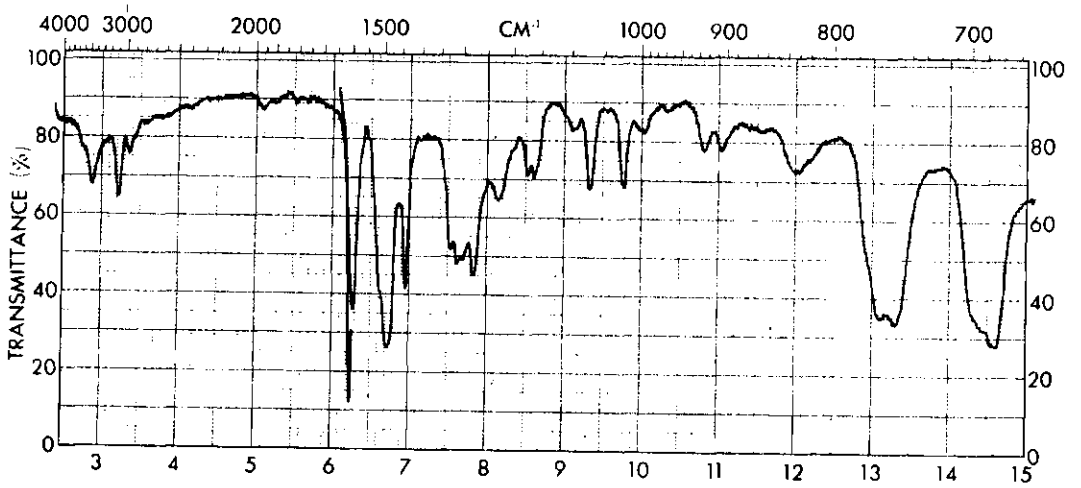

Figure 12. Oil from the Reaction of Diphenyliodonium Hydroxide with N-Phenylhydroxylamine (Neat)

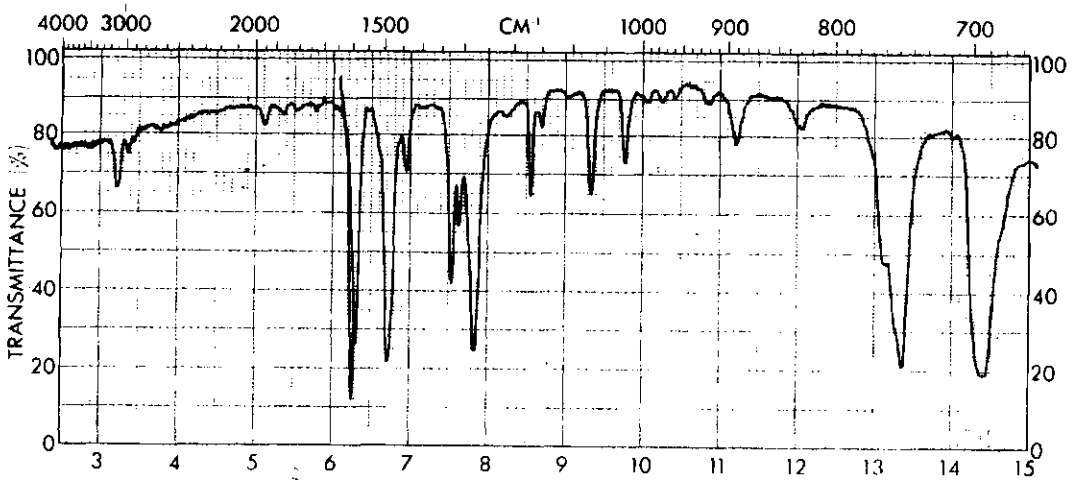

Figure 13. Triphenylamine from the Reaction of Diphenyliodonium Hydroxide with N-Phenylhydroxylamine (Thin Crystal Film)

CHAPTER III

DISCUSSION OF RESULTS

Attempted Phenylation of N-Acetylphenylhydroxylamine with Benzenediazonium-2-carboxylate

N-Acetylphenylhydroxylamine was chosen as a starting point for syntheses leading into the unknown series of O,N-diarylhydroxylamines since it is much more stable than N-phenylhydroxylamine, and since it was hoped to minimize reaction of the ambident nucleophile at nitrogen. Phenylation of N-acetylphenylhydroxylamine was attempted using benzenediazonium-2-carboxylate[42] as the phenylating agent. Stiles and Miller[42] have demonstrated that benzenediazonium-2-carboxylate phenylates a number of nucleophiles under mild conditions. These phenylations appear to occur *via* a benzyne intermediate, since Stiles and Miller[42] were able to trap it as a Diels-Alder adduct with furan and with anthracene. The existence of the benzyne intermediate from photolysis of benzenediazonium-2-carboxylate in the gas phase has been

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(42) M. Stiles and R. G. Miller, *J. Am. Chem. Soc.*, *82*, 3802 (1960).

clearly established by Berry, Spokes and Stiles.[43]

However, when phenylation of N-acetylphenylhydroxyamine was attempted by the addition of solid, freshly-prepared benzenediazonium-2-carboxylate to a benzene solution of the hydroxamic acid, the only isolable products were benzoic acid and acetanilide, each obtained in low yield. Polymeric tars and some unidentified oils accompanied these identified materials. The presence of benzoic acid among the products is easily rationalized by analogy with the ordinary course of homolytic diazonium ion decompositions under similar conditions.[44] The presence of acetanilide as a product is not as easily explained and may prove to be an artifact of the workup procedure. This matter may bear further investigation.

Phenylation of N-Acetylphenylhydroxylamine with Diphenyliodonium Hydroxide

The interesting work of Beringer, et. al.[35] on the chemistry of diaryliodonium salts as phenylating reagents suggested that treatment of N-acetylphenylhydroxylamine with a diphenyliodonium salt, followed by saponification, might

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(43) R. S. Berry, G. N. Spokes and M. Stiles, J. Am. Chem. Soc., 82, 5240 (1960).

(44) D. F. DeTar and M. N. Turetsky, J. Am. Chem. Soc., 77, 1745 (1955).

be a tractable approach to the synthesis of O,N-diphenylhydroxylamine. Diphenyliodonium bisulfate was chosen for its high solubility in water, and hence convenient conversion to the hydroxide.

The reaction between diphenyliodonium hydroxide (from the bisulfate) and N-acetylphenylhydroxylamine was carried out both in the presence and absence of atmospheric oxygen since Beringer and coworkers[45] have presented evidence that phenylations with diphenyliodonium salts have some free radical character. They suggest that phenylation may proceed by first a one-electron transfer from the nucleophile being phenylated to the diphenyliodonium ion in a loose complex between the nucleophile and the diphenyliodonium salt. Electron transfer is followed by loss of iodobenzene and combination of the radicals to yield the phenylation product. The presence of trace amounts of biphenyl in the products lends support for this mechanism.

When the phenylation reaction was attempted with or without the presence of atmospheric oxygen there were isolated both 4'-and 2'-hydroxy-4-N-acetylbiphenylamine (IV, V). Other products, which have not yet been identified, were

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(45) F. M. Beringer, S. A. Galton and S. J. Huang, J. Am. Chem. Soc., 84, 2819 (1962).

present but probably in smaller yield. The yield of the two biphenyl derivatives appears to be greatly improved by the exclusion of oxygen from the reaction mixture and the products of reaction are less complex. Thirty per cent of IV and an undetermined amount of V was found in the absence of oxygen and 8.6 per cent of III and 9.4 per cent of V in the presence of oxygen.

The isolation of the unexpected products IV and V as the major products of reaction under the mild, nonacidic isolation conditions suggests that the intended phenylation of N-acetylphenylhydroxylamine was accomplished and the desired product, N-acetyl-O,N-diphenylhydroxylamine, was formed, but spontaneously rearranged to IV and V. The probability that phenol or phenoxide ion derived from the decomposition of diphenyliodonium hydroxide is an intermediate in the reaction was reduced by determining the rate of disappearance of hydroxide ion from a solution of diphenyliodonium hydroxide under conditions identical to those of the phenylation reaction, except for the absence of N-acetylphenylhydroxylamine. Only 3.3 per cent of the diphenyliodonium hydroxide had decomposed after two days, far less than that required to explain the yields of IV and V, unless a polar, chain reaction utilizing catalytic amounts of phenol

as a chain-carrying species accounted for the rearrangement.[46] An aqueous solution of N-acetylphenylhydroxylamine, phenol and an equivalent of sodium hydroxide did not precipitate any products on standing for several weeks. The fact that the infrared spectrum (fig. 2), of the crude reaction mixture is identical with that of a mixture of purified IV and V suggests strongly that the formation of IV and V took place in solution and that they are not artifacts of the workup procedure. The pH of the reaction mixture never became more acidic than pH 7 during the entire course of the reaction, which fact makes the possibility of a proton-catalyzed process unlikely. It therefore appears that the most likely explanation of the formation of IV and V is that N-acetylphenylhydroxylamine anion was phenylated by diphenyliodonium ion to form the desired N-acetyl-O,N-diphenylhydroxylamine, which spontaneously rearranged to IV and V through a π-complex similar to that proposed by Dewar[16] for the benzidine rearrangement. This mechanism is represented on the next page (eqs. 18-20.) The possibility of forming IV and V directly from diphenyliodonium ion and N-acetylphenylhydroxylamine via a π-complex cannot be ruled out.

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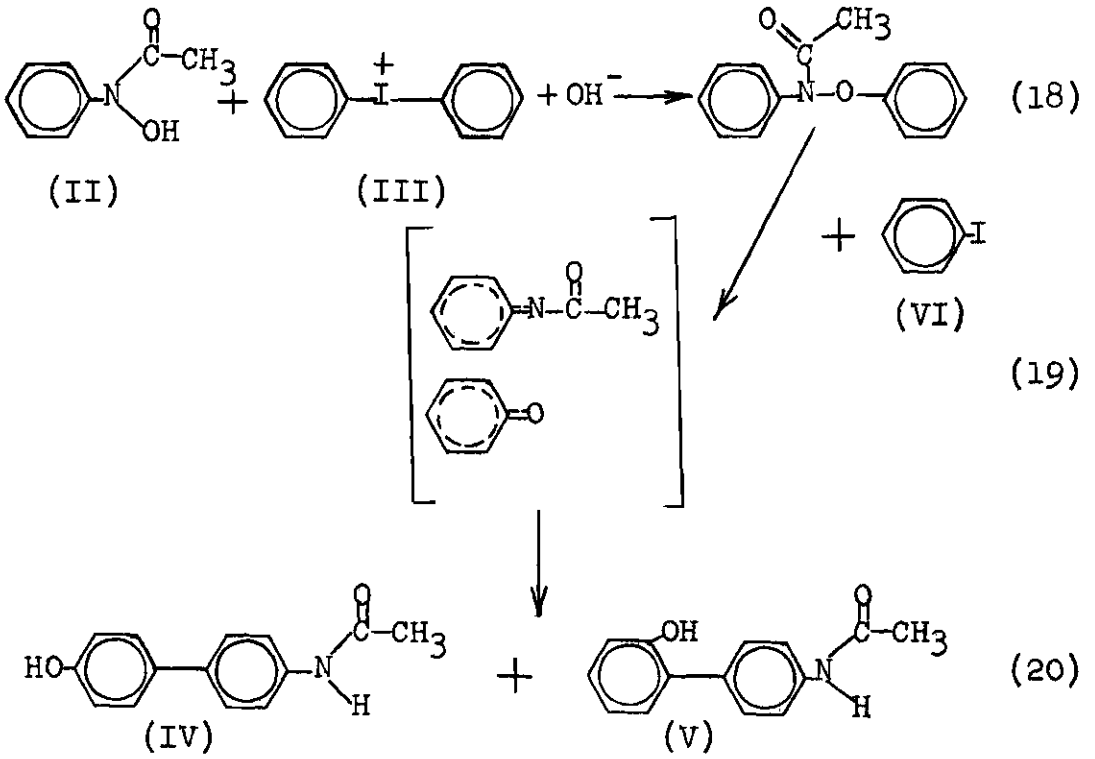
(46) We thank Prof. Jack Hine for suggesting this possibility.



If N-acetyl-O,N-diphenylhydroxylamine is indeed formed by the phenylation of the anion of N-acetylphenylhydroxylamine, its lability may be explained by analogy with the benzidine rearrangement. The electron-withdrawing inductive effect of the N-acetyl group may assume the role of the first proton in the benzidine rearrangement and that of the second proton may be partially fulfilled by the greater electronegativity of oxygen vis-à-vis nitrogen. Indeed, the possibility of a benzidine-like rearrangement in the absence of hydrogen ion catalysis is not unreasonable in view of the thermally induced benzidine-like rearrangements studied by Shine and Trisler.[22]

Attempted Phenylation of N-Phenylhydroxylamine with Diphenyliodonium Hydroxide

The interesting results obtained from the experiments with N-acetylphenylhydroxylamine and diphenyliodonium hydroxide demanded that phenylation of N-phenylhydroxylamine under identical conditions be attempted.

When N-phenylhydroxylamine was treated under conditions identical to those used in the attempted phenylation of N-acetylphenylhydroxylamine with diphenyliodonium hydroxide there resulted after 20 hrs. a yellow-brown oil from which there was obtained iodobenzene in 61 per cent of theory and triphenylamine in an amount sufficient to account for 11 per cent of the N-phenylhydroxylamine and 22 per cent of the diphenyliodonium hydroxide. The remainder of the reaction mixture appeared to be a complex mixture since chromatography over neutral alumina gave at least six visible bands when chloroform was the eluent.

It is then evident that phenylation of N-phenylhydroxylamine under these conditions can at best give only low yields of the desired product O,N-diphenylhydroxylamine due to the extensive formation of side products from decomposition of N-phenylhydroxylamine.

CHAPTER IV

CONCLUSIONS

The attempted synthesis of N-acetyl-O,N-diphenylamine by the phenylation of N-acetylphenylhydroxylamine with benzene diazonium-2-carboxylate in benzene results in polymeric tar formation. The formation of benzoic acid in low yield is rationalized as arising via a homolytic mode of diazonium salt decomposition analogous to the well known but poorly understood reductions of diazonium salts. The formation of acetanilide in low yield is not readily rationalized and may be an artifact of the isolation procedure.

The phenylation of N-acetylphenylhydroxylamine with diphenyliodonium hydroxide in the absence of atmospheric oxygen yields 4'-hydroxy-4-N-acetylbiphenylamine in 30 per cent of theory and some material which appears to be 2'-hydroxy-4-N-acetylbiphenylamine on the basis of its infrared spectrum and melting point. The nonacidic conditions of the phenylation reaction and isolation procedure make an acid-catalyzed mechanism unattractive. These results are rationalized herein as phenylation of the anion of N-acetylphenylhydroxylamine to form the presumably highly labile N-acetyl-

O,N-diphenylhydroxylamine which spontaneously rearranges to the observed products *via* an intramolecular pathway probably proceeding through a π-complex similar to that proposed for the benzidine rearrangement by Dewar.[16]

The reaction of N-phenylhydroxylamine with diphenyliodonium hydroxide leads to the extensive formation of side products due to the lability of N-phenylhydroxylamine. The only material other than iodobenzene yet isolated from the degassed reaction mixture was triphenylamine in 22 per cent of theory.

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